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10/586,337	07/14/2006	Akira Nishiyama	Q95734	2433
23373 7590 02/18/2010 SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037				
EXAMINER KELLY, ROBERT M				
ART UNIT		PAPER NUMBER		
1633				
NOTIFICATION DATE		DELIVERY MODE		
02/18/2010		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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### Office Action Summary

**Application No.**

10/586,337

**Applicant(s)**

NISHIYAMA ET AL.

**Examiner**

ROBERT M. KELLY

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 October 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 6 and 10-14 is/are pending in the application.
- 4a) Of the above claim(s) 11, 12 and 14 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1, 6, 13 is/are allowed.
- 6) ☒ Claim(s) 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S5108)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's amendment and argument of 10/26/09 are entered.

Claims 1, 6, and 13 are amended.

Claims 15 is cancelled.

Claims 1, 6, and 10-14 are presently pending.

### ***Election/Restrictions***

Claims 11-12, and 14 remain/are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonselected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/16/07.

Claim 6 is rejoined, as the broad claim is found otherwise allowable.

Claims 1, 6, 10, and 13 are presently considered.

### ***Claim Status—Cancelled Claims***

In light of the cancellation of Claim 15, all prior rejections and/or objections to such claims are withdrawn.

### ***Claim Objections***

In light of the amendment to Claim 13, the objection to such claim is withdrawn.

To wit, the amendment complies with the Examiner's suggestion to overcome the problem.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of the amendment to Claim 13 the rejection to such claim under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn.

To wit, Applicant has amended to remove the term “optionally”.

***Claim Rejections - 35 USC § 112 – new matter***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendment, the rejections of Claims 1, 10, and 15 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for being new matter, is withdrawn.

To wit, the claims now require the use of a reducing enzyme encoded by the Markush group of vectors.

***Claim Rejections - 35 USC § 112 - new matter***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 1 and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for comprising new matter, are withdrawn.

To wit, Applicant's amendment removes the various generic reducing enzymes and the non-possessioned organisms.

***Claim Rejections - 35 USC § 112 – new matter***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 13 is drawn to the enzymatic or non-enzymatic reduction of an aqueous solution of 5-hydroxy-2-pentanone-containing product of the acid hydrolysis of 2-acetyl-gamma-butyrolactone. The specification contains no guidance to limit the non-enzymatic reductions to aqueous solutions of such product obtained, either explicit, or implicit. In fact, much of what is utilized for such reductions is taught to be performed with compounds which specifically require the absence of water, e.g.,  $\text{LiAlH}_4$ . Further, there is no discussion or guidance with regard to performing such enzymatic reductions in the acidic aqueous solution presently claimed, the only

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examples are to such enzymatic, and yet neutralize the solution, and it is a truism that the enzymes would not be stable in such acidic conditions.

Moreover, Applicant provides no specific demonstration of possession of such, either explicit or implicit within the specification, as is their duty.

Hence, the Artisan would not have understood Applicant to have been in possession of the invention as claimed at the time of invention.

***Claim Rejections - 35 USC § 112 - enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 13 encompasses the, in the important aspect, the (i) enzymatic (meaning biological-enzyme-catalyzed) and (ii) non-enzymatic (meaning chemically-catalyzed) reduction of the solution production of reduction of 2-acetyl-gamma-butyrolactone by acid hydrolysis, producing an aqueous acid solution of 5-hydroxy-2-pentanone. The claim specifically requires the acid-catalyzed aqueous solution to be reduced, i.e., the 5-hydroxy-2-pentanone cannot be isolated and then reduced.

With regard to the use of biological enzymes, it is well known that biological enzymes are not generally stable and affective at low pH. There are a plethora of studies in the Art demonstrating that enzymes are destabilized or their active groups are affected with pH. One example is the recognition by Goto, that one of the oldest known methods of denaturing proteins is by the addition of acids (e.g., Goto, et al. (1990) *Proc Natl Acad Sci, USA*, 87: 573-77, p. 573, first paragraph of the introduction). Moreover, Applicant's own examples demonstrate that prior to the addition of the biological enzyme, the 5-hydroxy-2-pentanone needs to be neutralized (e.g., Example 2).

With regard to the reduction of 5-hydroxy-2-pentanone acidic product with non-enzymatic mechanisms, Applicant's specification teaches several compounds which may be utilized, including Lithium Aluminum Hydride, which is specifically argued, and agreed to by the Examiner, to not be possible in the aqueous solution, and hence, even though taught, would require the Artisan to design a new method to perform such reductions in water-containing solution. Still further, another of the specifically disclosed reducing agents, optically active tartaric acid-sodium borohydride is generally ineffective in simple ketones, and is also ineffective with the D isomer (Yatagai, et al. (1990) *J Chem Soc Perkin Trans*, 4: 1826-1828). Still further, it appears that the same art demonstrates the use of THF solvent, not aqueous solvent (p. 1827). Hence, it would appear that the Artisan would have to perform the experiment to determine if the compound would work, and if it could be performed in the aqueous product of the previous reaction. Still further, the rhodium complexes of the Art only work with alpha amino esters and beta ketoesters (e.g., Yamada, et al. (2003) *Chem Eur J*, 9: 4485-09, p. 4485 and Fujii, et al. (1996) *Journal of the American Chemical Society*, 118: 2521-22, p. 2521).

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Moreover, no compound has been found of the plethora of broadly-encompassed compounds listed by Applicant (e.g., paragraphs 0035-0038) which can be used in an aqueous acid solution of the composition required, and would be reasonably predicted to work on the simple gamma keto alcohol claimed.

Therefore, the Artisan would have to experiment to determine if any of these embodiments would work, and such is considered undue as it amounts to inventing the claimed subject matter for Applicant.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

In light of the amendment, the rejection of Claim 13 under 35 U.S.C. 103(a) as being unpatentable over Whitney, et al. (1974) Advances in Chemistry, Vol. 130: 270-80 and the general knowledge in the art, as now further evidenced by pp. 680-81 and 853-54 of Morrison and Boyd's Organic Chemistry Text, 3rd Edition, by Allyn and Bacon, New York, NY., for reasons of record, is withdrawn.

To wit,  $\text{LiAlH}_4$  cannot be used in an aqueous solution due to its combustible nature.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 1, 10 and 13 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzymes encoded in pNTS1G, pNTFPG, pNTDRG1, pNTRS, and pNTRGG1, to produce R, R, R, S, and S enantiomers, respectively, does not reasonably provide enablement for the breadth of products (e.g., any crude extract, any lyophilized cells, any acetone-dried cells of a microorganisms, and any disrupted enzymes) and the breadth of any reducing enzyme from the organisms and the breadth of enantiomers for any particular source, for reasons of record, are withdrawn.

To wit, the amendments overcome the problems with the claims ambiguities leading to much more than the simple enzymes, and any isomer being obtained.

### *Conclusion*

Claims 11, 12, and 14 remain withdrawn as being drawn to non-elected inventions.

Claims 1, 6, and 10 are allowed.

Claim 13 remains rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/  
Primary Examiner, Art Unit 1633

